REMARKS

We thank the Examiner for redesignating the claims to more accurately reflect the categories upon which the claims were restricted.

Claims 7 and 13, line 2 of each, have been amended to delete "aldehyde" and replace it with the more particularized term, --aldose--. Support for this amendment is found in the specification at, for example, page 2, lines 22-24 and lines 28-29 and lines 32-34; page 3, lines 29-33; page 4, lines 16-17; page 5, lines 8 to page 6, line 6; and page 11, lines 19-20; and see original claims 7 and 13.

Each of claims 7 and 13 has been amended to delete the phrase at the end, namely, "or cell-free extract prepared from a microorganism belonging to the genus *Gluconobacter* which is capable of producing the aldehyde dehydrogenase having the above properties in the presence of an electron acceptor". Support for the amended claims is found in the specification at, for example, page 2, line 32-34; and in original claims 7 and 13. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01 (o) and (l).

Claim 7 has been amended to delete various unnecessary parentheses.

Claim 13 has been amended to delete reference to withdrawn claim 1. An amendment also adds the subject matter of claim 1 with reference to a purified aldehyde dehydrogenase used in the claimed process. Support for this amendment is found in the specification at, for example, page 2, lines 22-29; page 1, lines 14-25; and page 5, line 7 to page 8, line 6; and in original claim 13. (Id.)

Claim 11 is amended to delete "for the production of vitamin C and 2-keto-L-gulonic acid, respectively". Support for the amended claim is found in the specification at, for example, page 2, lines 18-21; and in original claim 11. (Id.)

Claim 12 is amended to revise the dependency from that of claim 7 to that of claim 11. Support for this amendment is found in the specification at, for example, page 3, lines 15-19; and in original claim 12. (Id.)

Claim 15 is amended to recite that the "purified aldehyde dehydrogenase is prepared from a cell-free extract from" *Gluconobacter oxydans*. Support for this amendment is found in the specification at, for example, page 8, line 25 to page 9, line 22. (Id.)

Claim 18 is cancelled, without prejudice.

Indefiniteness Rejection

Claims 7, 10-13, 15, 18, 21 and 22 were rejected under 35 USC § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Paper No. 20070831 at 2.)

In making the rejection, the Examiner asserted that "[c]laim 7 is vague, indefinite and confusing in the use of parenthesis". (Id.) In response, all parentheses except those within which the acronym PQQ is recited have been deleted. It is believed that the amended claim is sufficiently definite with respect to the use of parentheses.

The Examiner also asserted that "[c]aims 7 and 13 are confusing in lacking antecedent basis for 'the aldehyde' at line 2 or 3, respectively." (Id.) It is

submitted that the amendment replacing the word "aldehyde" with -- aldose -- renders this rejection moot.

The Examiner also asserted that "[c]laim 13 is incomplete as depending on a non-elected claim." (Id.) Claim 13 has been amended to delete reference to claim 1. Amended claim 13 is now in independent claim format. The rejection is now moot.

The Examiner also asserted that "[c]laims 11 and 12 do not find clear antecedent basis in claim 7 for the products produced." (Id. at 3.) The Examiner asked whether "dependency on claim 10 [was] intended". (Id.) To further prosecution in this matter, claim 11 has been amended to delete recitation of the produced products. Thus, the dependency of amended claim 11 to claim 7 is proper. The dependency of claim 12 has been amended, though, from that of claim 7 to that of claim 11. Providing antecedent reference to products produced is not necessary as the product produced at a given set of recited conditions (which recited conditions are in amended claim 11) is clearly recited in amended claim 12. In any event, antecedent basis for the products produced is already provided in claim 7 in which it is recited that the purified aldehyde dehydrogenase used according to the process has a physico-chemical property as recited in d), which is "[o]ptimum pH of from about 6.5 to about 8.0 for the production of vitamin C from L-sorbosone or optimum pH of about 9.0 for the production of 2-keto-L-gulonic acid from L-sorbosone". It is submitted that the rejection should be withdrawn.

The Examiner further contended that "[c]laims 11 and 18 are confusing in that the antecedent basis for "respectively" is unclear regarding pH and temperature." (Id.) The word "respectively" has been deleted from claim 11 as noted above, and claim 18 has been cancelled. Accordingly, withdrawal of the rejection is requested.

In addition, the Examiner contended that "[c]laims 7, 10-13, 15, 18, 21 and 22 are incomplete in the absence of a recovery step for the product produced." (Id.) Although the Examiner acknowledged that "[w]hile there is no specific rule or statutory requirement which specifically addresses the need for a recovery step in a process of preparing a composition", the Examiner still asserted that "it ... would be expected from conventional preparation processes that the product must be isolated or recovered. Thus, the claims fail to particularly point out and distinctly claim the 'complete' process since the recovery step is missing from the claims." (Id.)

Applicants respectfully traverse the rejection.

Applicants respectfully submit that the language of the amended claims is sufficient under 35 USC § 112, second paragraph. First, we note that claim 7 has been amended to replace "aldehyde" with -- aldose --.

The legal standard for definiteness is whether a claim reasonably apprises those of skill in the art of its scope. *In re Warmerdam*, 31 USPQ 2d 1754, 1759 (Fed. Cir. 1994). Here, the amended claims meet that standard by explicitly reciting "[a] process for producing a carboxylic acid and/or its lactone from its corresponding aldose which comprises contacting the aldose with the purified aldehyde dehydrogenase ..." The claims apprise what the invention ***is***, and 35 USC § 112, second paragraph, does not require that the claims recite every detail of ***how*** it can or should be done. And, as acknowledged by the Examiner, there is no legal requirement to recite a recovery step.

Furthermore, "In rejecting a claim under the second paragraph of section 112, ***it is incumbent on the Examiner to establish that one having ordinary skill in the art would not have been able to*** ascertain the scope of protection defined by the

claim when read in light of the supporting specification." *Ex parte Cordova*, 10 USPQ2d 1949, 1952 (Board of Pat. App. and Int. 1989), citing *In re Moore*, 169 USPQ 236 (CCPA 1971). The Examiner has failed to provide any reason to support the assertion that one skilled in the art would not find the present claims sufficient under 35 USC § 112, when viewed in light of the specification.

Reconsideration and withdrawal of the rejection is requested.

Obviousness Rejection

Claims 7,10-13,15,18, 21 and 22 were rejected under 35 U.S.C. § 103(a) as obvious over Asakura *et al.* US Patent No. 5,916,785 ("Asakura"). (Paper No. 20070831 at 3.)

Asakura discloses "a novel alcohol/aldehyde dehydro-genase ('AADH'), a process for producing the same and a process for producing aldehydes, carboxylic acids and ketones, especially 2-keto-L-gulconic acid ('2-KGA') utilizing said enzyme." Col. 1, lines 43-47. Asakura also discloses that "[t]he AADH provided by the present invention catalyzes the oxidation of alcohols and aldehydes, and is thus capable of producing the corresponding oxo group from alcohols, and carboxylic acids from aldehydes. More particularly, the AADH provided by the present invention catalyzes the oxidation of L-sorbose to 2-KGA via L-sorbosone. 2-KGA is an important intermediate for the production of vitamin C." Col. 1, lines 48-54. Asakura further discloses that "Gluconobacter oxydans DSM No. 4025 (FERM BP-3812) may be used in the present invention as a source of novel AADH. . . ". Col. 5, lines 31-34.

In making the rejection, the Examiner asserted that "[Asakura] disclose the production of carboxylic acid from an aldehyde using a purified aldehyde dehydrogenase or a cell-free extract from strain *Gluconobacter oxidans DSM* 4025, using the same conditions as claimed. See, e.g., col. 6, lines 14-20." (Paper No. 20070831 at 3.)

The Examiner acknowledged that "[t]he reference differs from the claimed invention in that the specific production of vitamin C is not disclosed." (Id. at 4.)

The Examiner contended, however, that "one of ordinary skill in the art would reasonably have expected at the time the claimed invention was made that the required biotransformation [would] occur using the cell extract from this strain, since it has been shown to be capable of the required production of carboxylic acids from aldehydes, and the required reaction is inherent in the identical strain." (Id.)

It is well settled that the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO should include evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and modify the document(s) relied on by the Examiner as evidence of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731-32 (2007) (the obviousness "***analysis should be made explicit***" and the teaching-suggestion-motivation test is "***a helpful insight***" for

determining obviousness) (emphasis added); *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). Moreover, the factual inquiry whether to modify document(s) must be thorough and searching. And, as is well settled, the teaching, motivation, or suggestion test should "***be based on objective evidence of record***." *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (emphasis added). *See also Examination Guidelines for Determining Obviousness*, 72 Fed. Reg. 57526, 57528 (October 10, 2007) ("The key to supporting any rejection under 35 USC § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.").

Respectfully, we submit that the rejection is devoid of a proper section 103 analysis in support of the proposed modification. All that is there are conclusory statements such as the assertion that "it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of [Asakura] by using a cell-free extract of *Gluconobacter oxidans DSM* 4025 to produce vitamin C by adjusting process conditions, if necessary, for the expected benefit of optimizing the production of this useful vitamin." (Paper No. 20070831 at 4.) The Examiner further concluded that "the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary." (Id.)

Here, what the rejection should have done, but did not, was to explain on the record ***why*** one skilled in this art would modify the disclosure of Asakura in the manner proposed by the Examiner to arrive at the claimed process. As is well settled, an Examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the

motivating force which would impel one skilled in the art to do what the patent applicant has done. *Takeda Chem. Indus., Ltd v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. June 28, 2007) (citing *KSR*) (indicating that "it remains necessary to identify ***some reason*** that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound") (emphasis added); *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993). But this is precisely what the Examiner has done here. Thus, the rejection is legally deficient and should be withdrawn for this reason alone.

Notwithstanding the legally insufficient nature of the rejection, we note that the rejection is also factually insufficient to support a rejection under § 103(a). In doing so we observe that obviousness cannot be based upon speculation, nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (CCPA 1970). When a conclusion of obviousness is not based upon facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (BPAI 1993). Further, "to establish *prima facie* obviousness of a claimed invention, ***all claim limitations must be taught or suggested by the prior art***." MPEP § 2143.03 (citing *In re Royka*, 180 USPQ 580 (CCPA 1974)) (emphasis added).

As noted above, claims 7 and 13 have been amended to recite "contacting the aldose with a purified aldehyde...". These claims have also been amended to delete the option of contacting the aldose with the recited cell free extract.

In claim 7, the purified aldehyde dehydrogenase is recited as "having the following physico-chemical properties:

a) Molecular weight of 100,000 ± 10,000 Da consisting of two homologous subunits or molecular weight of 150,000 ± 15,000 Da consisting of three homologous subunits, where each subunit has a molecular weight of 55,000 ± 2,000 Da;

b) Substrate specificity: active on aldehyde compounds,

c) Cofactor: pyrroloquinoline quinone (PQQ),

d) Optimum pH of from about 6.5 to about 8.0 for the production of vitamin C from L-sorbosone or optimum pH of about 9.0 for the production of 2-keto-L-gulonic acid from L-sorbosone,

e) Inhibitors: Co^{2+}, Cu^{2+}, Fe^{3+}, Ni^{2+}, Zn^{2+}, and monoiodoacetate.

In claim 13, the purified aldehyde dehydrogenase is recited as having the same physico-chemical properties as in claim 7, except that "Substrate Specificity;" is recited as "active on L-sorbosone, D-glucosone, D-glucose, D-xylose".

We submit that although Asakura discloses "the production of carboxylic acid from an aldehyde using a purified aldehyde dehydrogenase...", as asserted by the Examiner in Paper No. 20070831 at 3, the Examiner has missed the mark by failing to recognize that the enzyme disclosed in Asakura is ***not*** the novel purified aldehyde dehydrogenase recited in the present claims for use in a process for producing a carboxylic acid and/or its lactone from its corresponding aldose. Asakura discloses the following, *inter alia*, with respect to their AADH enzyme:

> The invention reported herein is a homogenous protein AADH produced by a microorganism of the genus Gluconobacter.... This AADH has a molecular weight of 135,000±5,000 daltons, and is composed of an alpha and beta subunit and a pyrroloquinoline quinone prosthetic group. The alpha subunit has a molecular weight of 64,500±2,000 daltons. The beta subunit has a molecular weight of 62,500±2,000 daltons. (Col. 2, lines 19-30.)

As the AADH enzyme of Asakura is an enzyme characterized as having a molecular weight of about 135 kDa with two subunits of about 64.5 and 62.5 kDa, respectively (Col. 2, lines 24-30), Asakura's enzyme clearly differs from the purified alcohol dehydrogenase recited in the present claims for use in the claimed process. Specifically, the characterized enzyme disclosed by Asakura cannot be the same as the purified aldehyde dehydrogenase recited in the claims which has a "[m]olecular weight of 100,000 ± 10,000 Da consisting of two homologous subunits or molecular weight of 150,000 ± 15,000 Da consisting of three homologous subunits, where each subunit has a molecular weight of 55,000 ± 2,000 Da". Because the overall molecular weights as well as subunit molecular weights differ, the purified aldehyde dehydrogenase in accordance with the present claims is not disclosed or suggested by Asakura.

There is no disclosure in Asakura of the purified alcohol dehydrogenase recited for used in accordance with the claimed process. Furthermore, there is no indication in Asakura of the existence of the enzyme in accordance with the present claims. Nor is there any suggestion or motivation to obtain or attempt to isolate such an enzyme for use in the claimed process for producing a carboxylic acid and/or its lactone from its corresponding aldose.

Asakura further discloses:

> The AADH provided by the present invention is useful as a catalyst for converting alcohols to corresponding oxo groups, such as aldehydes and ketones, and for converting aldehydes to carboxylic acids. This reaction wherein alcohols and aldehydes are oxidized, comprises the step of treating the alcohol or aldehyde by contact with the AADH enzyme described herein. This AADH enzyme is provided in

> either or [sic] homogenous form or in a non-homogenous form. When the alcohol aldehyde is treated by contact with a microorganism of the genus Gluconobacter, capable of producing the AADH described herein, or by contact with a cell-free extract of such microorganism, then the AADH is provided in a non-homogenous form. This AADH is especially useful for the production of 2-KGA from L-sorbose via L-sorbosone. (Col. 6, lines 6-20.)

In addition, Asakura discloses contacting an L-sorbose substrate with purified AADH at pH 6.5, and that "[a]s a result, 2-KGA was formed...". (Example 2 at Col. 8, lines 44-52.) Also, Asakura discloses contacting an L-sorbose substrate with cells of Gluconobacter oxydans DSM No. 4025 (FERM BP-3812), and that "[a]s a result, 2-KGA formation was observed...". (Example 3, Col. 8, lines 54-63.)

And, as noted above, Asakura discloses that "the AADH provided by the present invention catalyzes the oxidation of L-sorbose to 2-KGA via L-sorbosone. 2-KGA is an important intermediate for the production of vitamin C." Col. 1, lines 48-54.

In view of the cited portions of Asakura as well as the teachings of Asakura as a whole, one skilled in the art would understand that the AADH enzyme disclosed by Asakura is useful in the production of 2-KGA, an intermediate in the production of vitamin C. Thus, one skilled in the art would understand that to produce Vitamin C, a separate step would be necessary to convert the 2-KGA intermediate into Vitamin C.

One skilled in the art would ***not*** derive any motivation from Asakura, on the other hand, to use the AADH enzyme or to isolate any other enzyme from the same source to attempt a process capable of producing either or both a carboxylic acid such as 2-KGA and its lactone such as, e.g., Vitamin C, from its corresponding aldose, i.e.,

from the same substrate. Nor would one skilled in the art consider that the presently claimed process for producing a carboxylic acid and/or its lactone from its corresponding aldose would be expected or achievable, in view of the disclosure of Asakura.

To underscore the significance of the purified aldehyde dehydrogenase of the present claims, it has the dual function or ability that it can act on the same substrate, e.g. sorbose, to produce a carboxylic acid, e.g., 2-KGA, and/or its lactone, e.g., Vitamin C. Neither the enzyme nor its use in the claimed process is disclosed or suggested in any way by Asakura.

Moreover, ***the claimed process in which an aldose such as sorbose can be converted into its lactone such as Vitamin C in a single processing step and by the action of a single enzyme can be viewed as an important milestone for industrial production of Vitamin C.*** Certainly, no disclosure or suggestion is present in Asakura and the Examiner has provided no other evidence that would lead one skilled in the art to attempt the claimed process.

For the reasons provided, it is submitted that the rejection has been rendered moot.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims is respectfully requested.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on April 25, 2008.

Eileen M. Ebel, Reg. No. 37,316

Respectfully submitted,

By:

Eileen M. Ebel
Registration No. 37,316
BRYAN CAVE LLP
1290 Avenue of the Americas
New York, NY 10104-3300
Phone: (212) 541-2000
Fax: (212) 541-4630